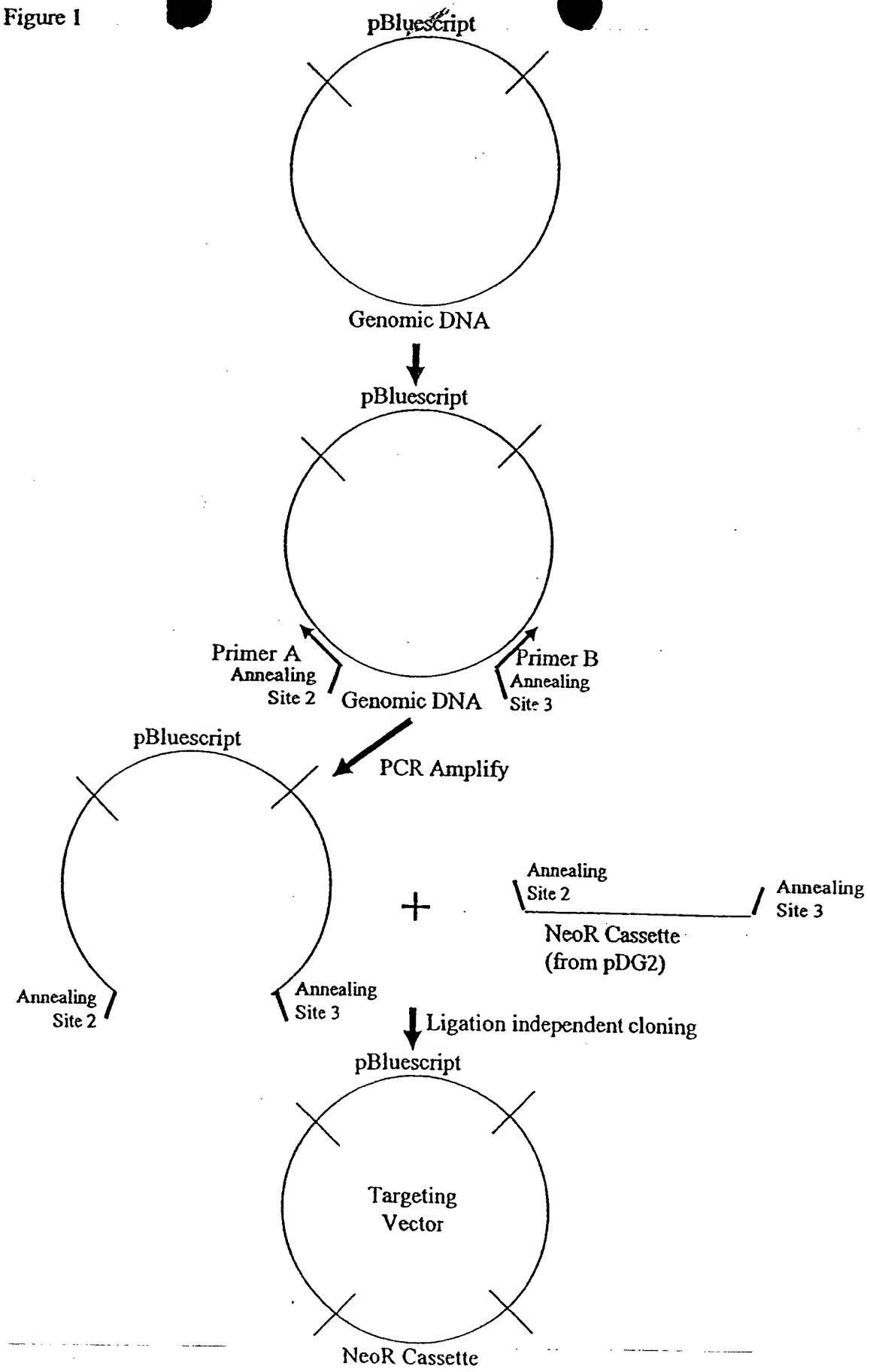


Figure 1



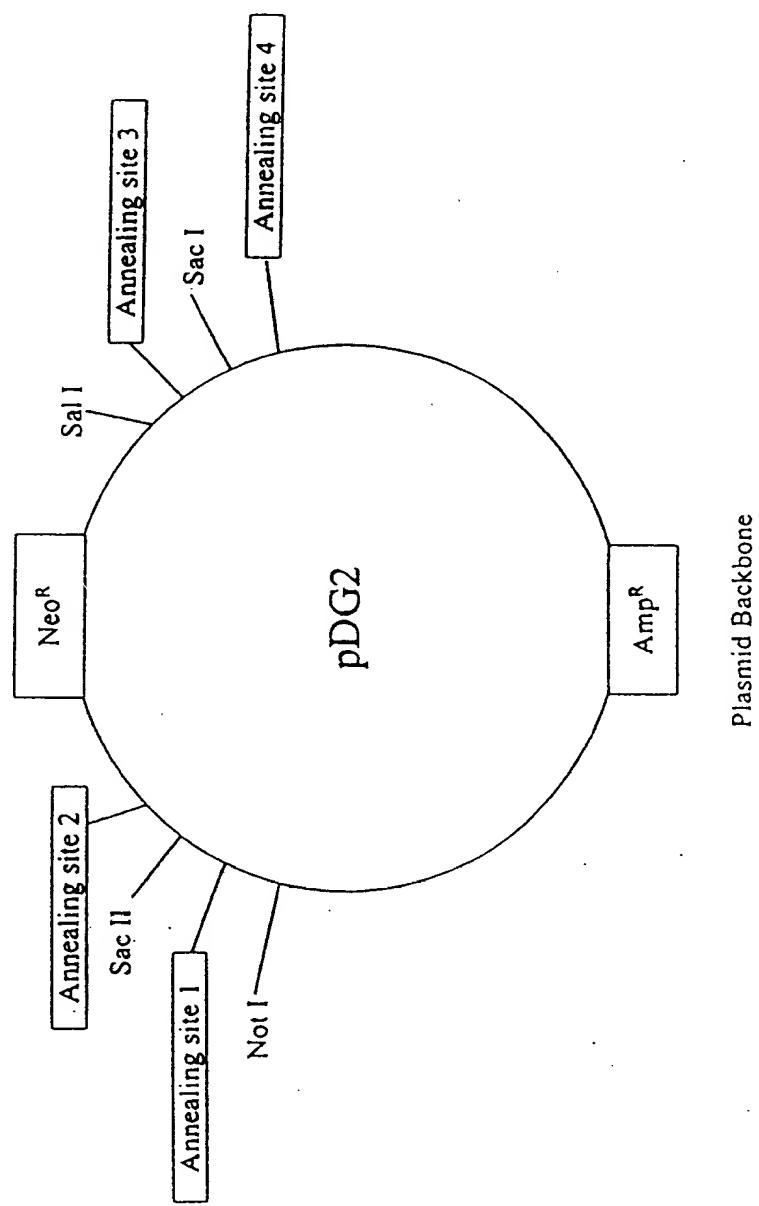


FIGURE 2A

FIGURE 2B

pDG2:

GTAACTACGTAGTGGCACTTTGGGAAATGTGCGCGAACCCATTGGTTATTTCTAAATACATTCAAAATA
TGTATCCGCTCATGAGACAATAACCTGATAAAATGCTCAATAATATTGAAAAGGAAGAGATGAGTATTCAACATTTC
CGTGTGCCCCCTATTCCCTTTGGCCTTGTCTGCTACCCAGAAACGCTGGTGAAGATCCTTGAGAGTTTCC
TGCTGAAGATCAGTTGGGTGACAGTGGGTTACATGAACTGGATCTCAACAGCGGTAAAGATCCTTGAGAGTTTCC
CCGAAGAACGTTCTCAATGATGAGCACTTTAAAGTCTGCTATGTGGCGGGTATTATCCGTGTTGACGCCGGCAA
GAGCAACTCGTCGCCGACACTATTCTCAGAATGACTTGGTGAAGTACTCACCAGTCACAGAAAAGCATCTTACCGA
TGGCATGACAGTAAGAGAAATTGCACTGCTGCCATAACCATGAGTGAATAACACTGCGGCCACTTACTTCTGACAACGA
TCGGAGGACCGAAGGAGCTAACCGTTTGGCACAACATGGGGATCATGTAACCTGCCCTGATCGTTGGAAACGGAG
CTGAATGAAGCCATACCAAAACGACGCGTGAACACACGATGCTGTGCAATGGCAACAAACGTTGCGCAAACACTATTAAAC
TGGCAACTTACTCTAGCTCCGGCAAAATTAAATAGACTGAGTGGAGGGATAAAAGTGCAGGACCCACTTC
GCTCGGCCCCCTCCGGCTGGCTGGTTATGCTGATAAAATCTGGAGCCGTAGCGTGGTATCGCGGATCATTGAGCA
CTGGGGCCAGATGTAAGCCCTCCGATCGTAGTTACTCACGACGGGAGTCAGGCAACTATGGATGAACGAAATAG
ACAGATCGCTGAGATAGGTGCTCACTGATTAAGCATTGGTAACGTCAGACCAAGTTACTCATATATACTTATAGTTG
ATTATACCCGGTTGATAATCAGAAAAGCCCCAAAACAGGAAGATTGATAAGCAAATTTAAATTGTAACGTTAA
TTTGTAAAATCGGTTAAATTGTTAAATCAGCTATTAAACCAATAGGCCAAATCGGAAAATCCCTAT
AAATCAAAGAAATAGCCCAGATAGGGTTGAGTGTGTTCCAGTTGGAAACAAGAGTCCACTATTAAAGAACGCGACTC
CAACGTCAAAGGGCGAAAAACCGCTATCAGGGCGATGGCCCACTACGTGAACCATACCCAAATCAAGTTTGGGGT
CGAGGTGCGTAAAGCATAATCGAACCCCTAAAGGAGCCCCGATTTAGAGCTGACGGGGAAAGCGAACGCTGGCGA
GAAAGGAAGGGAAGAAAGCGAAAGGAGCGGGCGTAGGGCGCTGGCAAGTGTAGCGGTACCGCTGCGCGTAACCA
CCCGCCGCGTTAATCGCCGCTACAGGGCGCTAAAAGGATCTAGGTGAAGATCCTTTGATAATCTCATGACCAAAA
TCCCTTAACGTGAGTTTCTTCACTGAGCGTAGACCCCGTAGAAAAGATCAAAGGATCTCTTGAGATCCTTTT
CTGCGCTAATCGCTGTTGCAAAACAAAACCCACCGCTACAGCGGTGGTTGTTGGGAGTCAGAGCTAC
TCTTTCCCGAAGGTAATGGCTTCAAGAGGGCAGATACCAAATACTGTTCTACTGTAGCCGTAGTTAGGCCACC
ACTTCAGAAGACTCTGAGCAGGCTACATCTGCTCTGTAATCTGTTACAGTGGCTGCTGCCAGTGGCATAAG
TCGTGCTTACGGGTTGACTCAAGCAGATAGTTACCGGATAAGGGCTGCGTGAACGGGGGTTCTGTCAC
ACAGCCCAGTTGGAGCGAACGACCTACACCGAACTGAGATACTTACAGCGTAGCTATGAGAAAGCGCACGCTTCC
AAGGGAGAAGGCGGACGGTATCCGTAAGCGCAGGGCTGGAAAGCGAGAGCGCACGAGGAGCTTCAGGGGAAAC
GCCGGTATCTTATGTCGGGTTCCGCCACCTCTGACTTGAGCGTCGATTTTGATGCTGTCAGGGGGCG
GAGCCTATGAAAAACGCCAGCAACCGGGCTTTTACGGTTCTGGCTTIGCTGGCTTIGCTCACATGTAATGTG
AGTTAGCTCACTCATTAGCACCCAGGTTTACACTTATGCTTGGCTCGTATGTTGTTGAGGATA
ACAATTTCACACAGGAAACAGCTATGACCATGATTACGCCAAGCTACGTAATACGACTCACTAGCGGCCGTTAAAC
AATGTCCTCTTGGCTGCTTCCGGGCAAGCCAGACAAGAACAGTTGACGTCAAGCTCCGGGACCGTGCT
AGCGCGCGCCGAATTCTGAGGATTGAGGGCCCTGAGGTCAATTCTACCGGGTAGGGAGGCGCTTCCCAAGG
CACTCTGGAGCATCGCTTAGCAGCCCGCTGGCACTTGGCTACACAAGTGGCTCTGGCTCGCACACATTCCACA
TCCACCGTAGCGCCAACCGCTCCGTTTGGGGCCCTTGGCCACCTTCACTCTCCCTAGTCAGGAAGTTC
CCCCCGCCCGCAGCTCGCTGTCAGGACCTGACAATGGAGTACGACGTCTCACTACGCTGCAAGTGGACAG
CACCGCTGAGCAATGGAGCGGGTAGGCCCTGGGCGACGGGCAATAGCAGCTTCTGCTCTCGCTTCTGGCTCAGA
GGCTGGAGGGGTGGCTGGGGGGGGCTCAGGGGGGGCTCAGGGGGGGGGGGCGGAAGGTGGCTCTGGGAGGCC
GGCATTCTCGCACGCTTAAAGCGCACGCTGCGCTGTTCTCTCTCATCTCCGGGCTTTCGACCTGAGC
CAATATGGGATCGGCCATTGAAACAGATGGATTGCAAGCAGGTTCTCCGGCCCTTGGGGAGGCTATTGGCTATG
ACTGGCACAACAGACAATCGGCTGCTGATGCCCGTGTCCGGCTGTCAGCGCAGGGGCCGCGTATCGTGGCTGCCAC
AAGACCGACTGTCGGTGGCCCTGAATGAACTGCAAGGACGAGGAGCGCCGCTATCGTGGCTGCCACGACGGGTTCC
TTGCGCAGCTGTGCTGAGCTGTAACGAGGGAAAGGGACTGGCTGCTATTGGCGAAGTGCAGGGGAGGATCTCC
TGTCTCATCTACCTTGCTCTGGAGAAAGTATCCATCATGGCTGATGCAATGCGCGGCTGCATACGCTTGTGATCC
ACCTGCCCATCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTAACGGATGGAAGCCGGTCTTGTGATCAGGA
TGATCTGGACGAAGAGCATCAGGGCTCGGCCAGCGAATCTGCTGCTCTGGCAAGGCTCAAGGCCGATGCCGACGGCATG
ATCTCTGCTGACCCATGGCATGCTGCTTGGCAATATCATGGTGGAAATGGCCGTTTCTGATTATCATGACTGT
GGCGCGTGGGTGTTGCGGAGCGCTATCAGGACATAGCGTTGGCTACCGTGATATTGCTGAAGAGCTGGCGGAATG
GGCTGACCGCTTCTGCTGTTACGGTATGCCGCTCCGATTGCGCATCGCCTTATGCCCTTCTGACGAGT
TCTTCTGAGGGGATCGATCGCTCTGTAAGTCTGAGAAATTGATGATCTATTAAACAATAAGATGTCACAAATGG
AAGTTTCTGTCATAATTGTTAAAGAAGGGTGAAGAACAGAGTACCTACATTGAAATGGAAGGATTGGAGCTACGGGG
GTGGGGGTGGGGGGATAGATAAACTGCCCTTACTGAGGGCTTACTATTGCTTATGATAATGTTCTAG
TTGGATATCATATAATTAAACAGCAAACCAATTAAAGGGCCAGCTCATTCTCCACTCATGATCTATAGATCTATAGA
TCTCTGCTGGGATCATTGTTTCTGTTGATGCCACTTGTGTTCTAAGTCTGTTTCTGTTTCAAAATGTCAGTTCA
TAGCTGAGGAACGAGATCAGCAGCCTCTGTTCCACATACCTCATTCTCAGTATTGTTGCAAGTCTAATTCCAT
CAGAAGCTGACTCTAGATCTGGATCCGGCAGCTAGGCCGTCAGCTGAGTCAAGGACCGTCTCGCTCTG
TCCGTTGAGCTGACGACACAGGACACGCAAATTAAATTAAAGGCCGGCCGACCGTACGCCCTTCACTGCAAGGCTTAAGTGA
TATTACCGACTGGCCGCTGTTTACAACGTCGTGACTGGAAAACCCCTGGCTTACCCAACTTAATGCCCTGCGACA
TCCCCCTTCCGCACTGGCGTAAAGCGAAGAGGCCGACCGATGCCCTTCCAAACAGTGCAGGCCGATGGCG
AATGGCGCTTGGTAATAAGGCCGCTTGGGCTTGGGTTTTTTTT

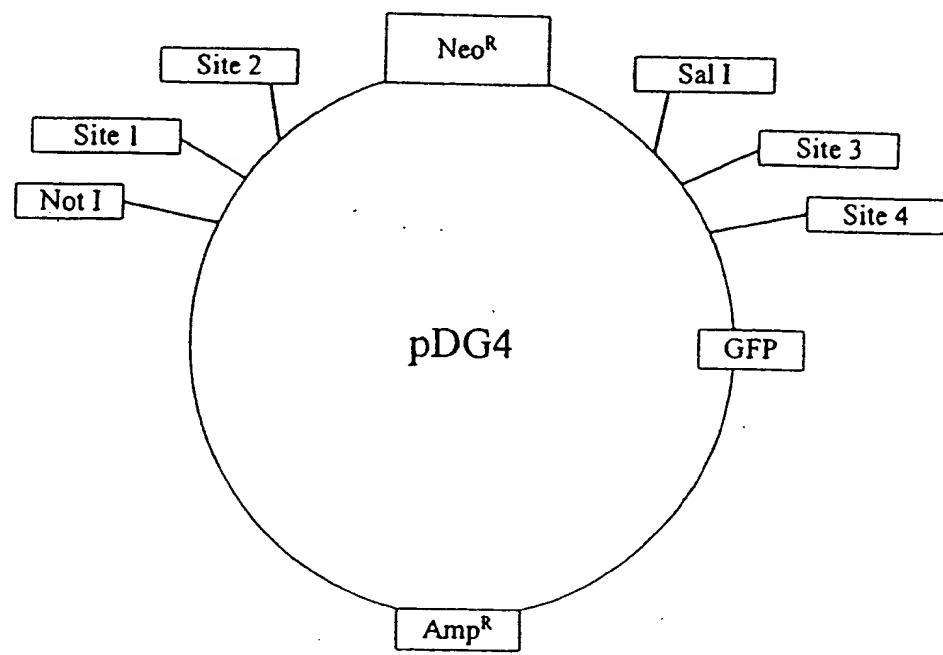


FIGURE 3A

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FIGURE 3B

pDG43

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TGCTCCTGCCGAGAAAGTATCCATATGGCTATGCAATGCCGGCTGCATACGCTTGATCCGGTACCTGCCATTG
ACCACCAAGCGAAACATCGCATCGAGCGACGTACTCGGATGGAAGCCGGCTTGCGATCAGGATGATCTGGACGAA
GAGCATCAGGGGCTCGCGCCAGCGAACCTGTCGCCAGGCTCAAGGCGCGATGCCCGACGGCGATGATCTCGTCGTGAC
CCATGGCGATGCCCTGCTTGCCTGAATATCATGGTGGAAAATGCCGCTTTCTGGATTATCGACTGTGGCCGGCTGGGTG
TGGCGGACCGCTATCAGGACATAGCGTGGCTACCCGTGATATTGCTGAACAGCTTGGCCGGAAATGGCGTACCGCTTC
CTCGTGCCTTACGGTATCGCCGCTCCGATTGCGAGCGCATGCCCTCTATGCCCTCTGACGAGTTCTGAGGGGA
TCGATCCGTCCTGTAAGTCTGCGAGAAATTGATGATCTATTAAACAATAAAAGATGTCACAAATGGAAGTTTCTCTG
CATACTTGTTAAGAAGGGTGAGAACAGAGTACCTACATTTGAATGGAAGGATTGGAGCTACGGGGGGGGGGGGGG
GGGATTAGATAAATGCTGCTCTTACTGAAGGTCTTACTATTGCTTATGATAATGTTCATAGTTGGATATCATAA
TTAAACAAGCAAACCAAATTAAAGGCCAGCTCATGCCCTCCACTCATGATCTATAGATCTATAGATCTCTGTTG
CATGTTTCTCTGATTCCACTTGTGGTTCTAAGTACTGTGGTTCCAATGTCAGTTCTATGCCCTGAGAAC
GAGATCAGCAGCCCTCTGTTCCACATACACTCATTCTCAGTATTGTTTCCAAGGTTCTAATTCCATCAGAACGCTGACTC
TAGATCTGGATCCGGCAGCTAGGCCGTGACCTCGAGTGAATCAGGTACCAAGGTCTCGCTCTGTTGGCTGAGCTCG
ACGACACAGGACAGCAAATTAAATTAAAGGCCGGCCGTACCCCTAGTCAGGCTTAAGTGAATGTCGTTACCGACTGG
CCGTGTTTACAACGCTGACTGGAAAACCCCTGGCGTTACCCAACTTAATGCCCTGAGCACATCCCCCTTCGCC
AGCTGGCGTAATAGCGAAGAGGCCGACCGATGCCCTCCAAACAGTTGCGCAGCCTGAATGGCGAATGGCGCTTCGC
TTGGTAATAAGCCGCTCGCGGGCTTTTTTT

FIGURE 3B (Continuted)

09816260 032304

Annealing site	Sequence	Sequence after digestion
1	5' tggctcccttggctgtccaa... 3' 3' acacgaggaaaccgaaacggaaaggtt... 5'	5' tggctcccttggctgtccaa... 3' 3' tt... 5'
2	5' ctggttttgtctggcttggcccaa... 3' 3' gaccaaggaaacacggaaaccgggtt... 5'	5' ctggttttgtctggcttggcccaa... 3' 3' tt... 5'
3	5' ggtccctcgctctgtccgttgtgaa... 3' 3' ccaggaggcgagacacaggcaactt... 5'	5' ggtccctcgctctgtccgttgtgaa... 3' 3' tt... 5'
4	5' ttggcggtctgtgtcgtcgaa... 3' 3' aaacggcacaggacacaggcaggctt... 5'	5' ttggcggtctgtgtcgtcgaa... 3' 3' tt... 5'

FIGURE 4

Annealing site	Sequence	Sequence after digestion
1	5' AAtgtgctctttggcttccgc 3'	5' AA 3'
	3' Ttacacgaggaaaacccaaacgaaagg 5'	3' Ttacacgaggaaaacccaaacgaaagg 5'
2	5' AActggttcttgtctggccgc 3'	5' AA 3'
	3' Ttgaccaaaacgacccaaacgggg 5'	3' Ttgaccaaaacgacccaaacgggg 5'
3	5' AAGtccctcgcttgtccgttgAGCT 3'	5' AA 3'
	3' Ttcaggaggcgagacacaggcaac 5'	3' Ttcaggaggcgagacacaggcaac 5'
4	5' AAttggcggtccctgtgtcgTCGAGCT 3'	5' AA 3'
	3' Ttaaacggcacaggacacaggcagg 5'	3' Ttaaacggcacaggacacaggcagg 5'

FIGURE 5

FIGURE 6

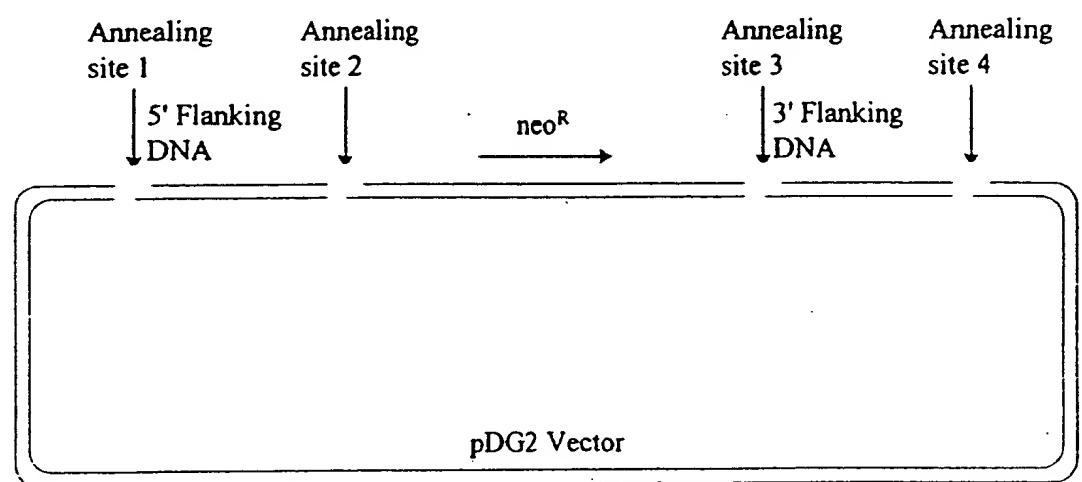
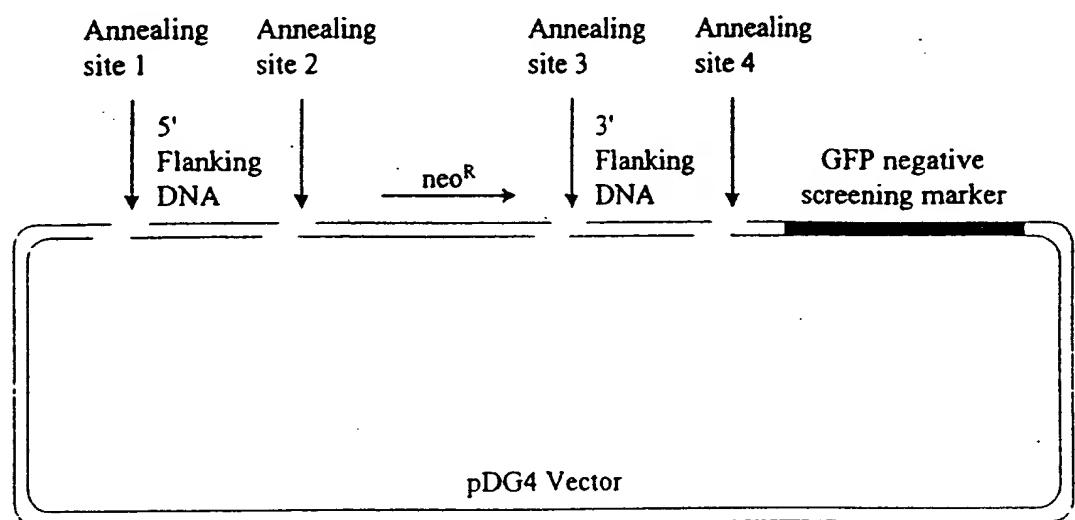


FIGURE 7



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09056790 " 03204
TCCCCACATTGCAAAGCCTACACAAAGATCCCTACCACTGAGCACCAGGGAGGCATGGCTCAGAACCC
AGCAACATGGAGCCCTGCGTAAACCACTGGCCTGTGAAGGGATCCACTCATCAAATACTTGC
AGACAATGGAGCAACTGCAGAACTTCACAGCCTGGCCTGATGATGTGCTCATCAGCAC
TGGTACTAATGGATGAGTGAGATCATGGATATGATCTATCAGGGTGGCAAGCTAGATAAG
TGGTGGCCGG
GCCCGTCTATGCCGGATACCCCTCCTGAGGTTAGCTGCCAGGGTCCCCCAGGTCTGAAACTC
TGAAAGAGACACCAGCCCCACGGATCATTAAGACACATCTGCCCTGCTTACTCCCTCAGAGTCTG
GGATCAAAAGATCAAGGTGATCTACGTTGCCGAAATGCAAAGGATGTTGCTCTATTATAACTC
TACAAAATGGCCAAGCTGCACCCCTGACCCAGGCACCTGGAAAGCTTCTGGAGAAC
AAAGTGCCTATGGGCGTGGTACCAAGCACGTGAAGGAGTGGAGCTGAGACGC
ACTCACCCCTGTTCT
CTATCTCTTCTATGAAGACATGAAGGAGAATCCAAAGGGAGATCAAGAAGATTCTAGAGTTCTGGGG
CGCTCTACCTGAGGAGACTGTGGATTTAATGTTCACCA
CACATCCTCAAGAAAATGAAGGAGAAC
CCATGGCTAACTACACAACC
ATCCAACTGAAGTTATGGACCACACTATT
TATCCCTCATGAGGAAGG
TACCAATTGGGACTGGAAAATAC
CTTCACTGTAG
GCCAGAGTGAGCACTTTGATGCC
ACTATGCCAAG
CTAATGACAGGTTGTGACTTCACGTTCCGCTGTCAA
ATATGAATTG
GGATATGGCTATACTGGGAACCA
AGGCAAGCTGACACAT
CCCCCAT
GTGATCTCAAGAGAAAATGTGATGTT
CATATTGTT
TATGCCT
AAAGGAAATCTGAGCTAAGAGAATAGGACTGGG
GATGCTGAGG
CAGGGTCTTATGAACATGTCAGG
AAAGCCATCAGT
CCTAACACTG
AAAAGAAC
CTAAAGTAC
AAACATG
AAAAAATAG
TAAGATAAA
CTGTA
TTTAC
CTGAAC
AAATAA
ATGCC
ACTGGG
AGCTG
ACTGG
(SEQ ID NO: 19)

Targeting Vector (5' arm; 200 bp flanking neo insert):

AGAACCCCTGCCCTACTCCACCTCCTCCCTTTTGTGAGAACAGCCAGTC
TAGCACTGTTCCACTTCCCTCCACTGGGACACAAAATCTCCAGCTCAAAGACCAATTCTG
CATTCCCCACATTGCAAAGCCTACACAAAGATCCCTACCACTGAGCACCAGGGAGG
CATGGCTCAGAACCCAGCAACATG
(SEQ ID NO: 20)

Targeting Vector (3' arm; 200 bp flanking neo insert):

AGGGTGGCAAGCTAGATAAGTGTGGCCGGGCCCCGTCTATGCCGGATACCCTCC
TTGAGTTCA
GCTGCCAGGGTCCCCCAGGTATGTG
CATGGGGTGTAGAGACAA
GTGGAAAAGGTAGGACC
GGGGCCCCAGTTAAC
AAAGTTCC
TTGTTCAACTTAGGTCT
TGAAACTCTGAAAGAGACACCAGCCCCA
(SEQ ID NO: 21)

FIG. 8